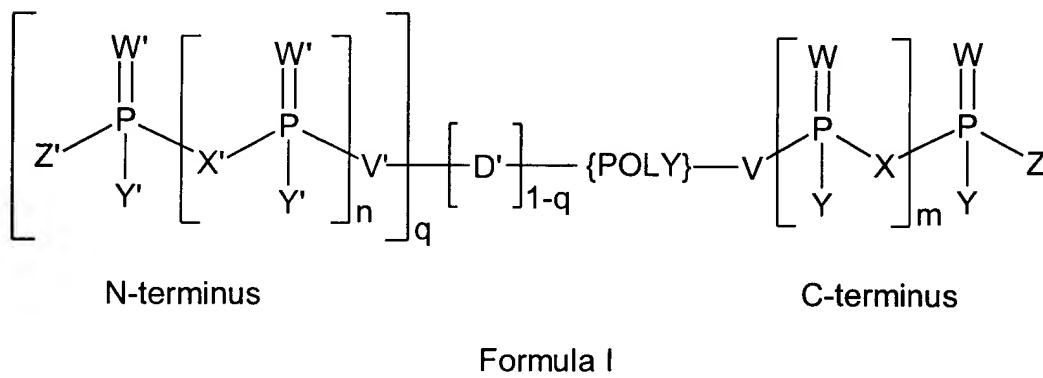


What is Claimed is:

1. A PNA derivative which carries one or more phosphoryl radicals at the C terminus or at the C and N termini of the PNA backbone, wherein the phosphoryl radicals comprise oxo-, thio- and imino-phosphoryl radicals, and wherein at least one of the phosphoryl radicals carries one or more deprotonatable groups, -and wherein the phosphoryl radicals are linked to the PNA backbone by way of an oxygen-phosphorus bond, a sulfur-phosphorus bond or a nitrogen-phosphorus bond, either directly or by way of a spacer.
 2. A PNA derivative as claimed in claim 1, wherein the spacer is an alkanoylamide, a poly(alkoxy)carboxamide, or an amino acid.
 3. A PNA derivative of Formula I



wherein

q is 0 or 1;

D' is, independently of each other, hydroxyl, mercapto, amino, alkylamino, or acylamino;

V is oxygen, sulfur, or NR_1 ;

V' is, independently of any other V', oxygen, sulfur, NR₁, U-(CR₃R₄)_{u'}-C(O)-NH, or U-(CH₂CH₂O)_{u'}-CH₂-C(O)-NH;

U is, independently of any other U, oxygen, sulfur, or NH;

u' is, independently of any other u', from 1 to 10;

W and W' are, independently of each other, oxygen, sulfur, or NR₁;

Y and Y' are, independently of each other, hydroxyl, mercapto, oxyanion, thioate, or NR₁R₂;

X and X' are, independently of each other,

U-(C₂-C₂₂-alkanediyl)-U,

U-(CH₂CH₂-O)_{u'},

a labeling group,

a group for crosslinking,

a group which promotes intracellular uptake, or

a group which increases the binding affinity of the PNA derivative for nucleic acids;

Z and Z' are, independently of each other,

hydroxyl,

mercapto,

oxyanion,

thioate,

NR₁R₂,

C₁-C₂₂-alkyl,

C₁-C₈-arylalkyl,

C₁-C₂₂-alkyl-U,
C₁-C₈-arylalkyl-U,
hydroxy-C₁-C₁₈-U,
aminoalkyl-U,
mercaptoalkyl-U,
a group of the formula R₇(CH₂CH₂-O)_{m'}, wherein R₇ is hydroxyl, amino, or C₁-C₂₂-alkoxy, and m' is from 1 to 100,
a labeling group,
a crosslinking group,
a group which promotes intracellular uptake, or
a group which increases the binding affinity of the PNA derivative for nucleic acids;

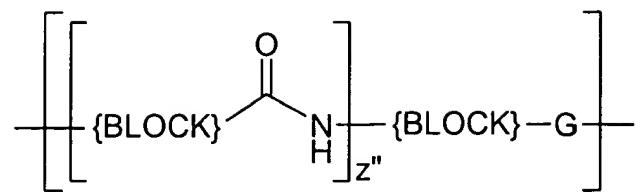
R₁ and R₂ are, independently of each other, a radical consisting of hydrogen or C₁-C₆-alkyl, preferably hydrogen,

R₃ and R₄ are, independently of each other, a radical consisting of hydrogen or C₁-C₆-alkyl, or the radical of an amino acid side chain, wherein adjacent radicals R₃ and R₄ in V' can also form a C₅-C₈-cycloalkyl ring;

n is from 0 to 10;

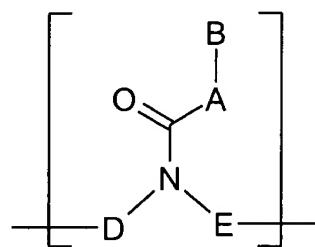
m is from 0 to 10;

and wherein {POLY} is described by Formula II



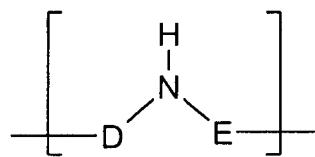
Formula II

wherein {BLOCK} is, independently of any other {BLOCK}, a group selected from Formula IIIA,



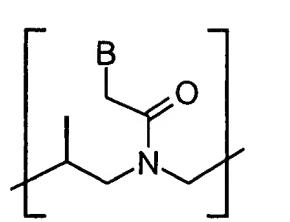
Formula IIIA

Formula IIIB,

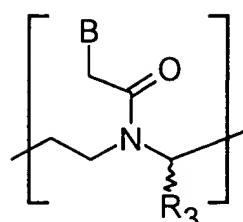


Formula IIIB

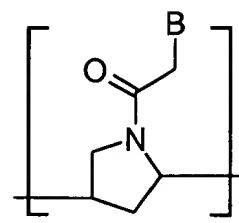
and Formulae IV A to IV G,



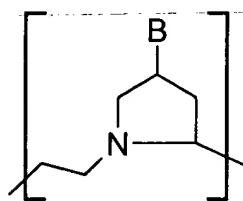
Formula IV A



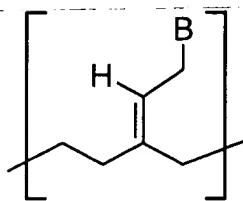
Formula IV



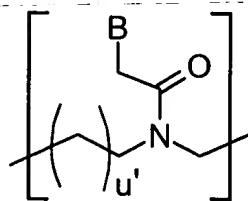
Formula IV C



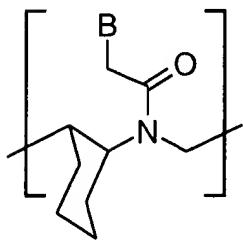
Formula IV D



Formula IV E



Formula IV F



Formula IV G

wherein each {BLOCK} building block can be different,

and wherein

z'' is from 0 to 100;

G is $(CR_5R_6)_{u'}$, $C(O)NH-(CR_1R_2)_{t'}$, or $C(O)NH-(CH_2CH_2O)_{u'}-CH_2CH_2$,
wherein t' is from 2 to 10;

A is, independently of any other A, a group $(CR_1R_2)_s$, wherein s is from 1 to 3;

B is, independently of any other B, either
an aromatic radical, a heteroaromatic radical, hydrogen, hydroxyl, or

C₁-C₁₈-alkyl, or

a nucleobase which occurs naturally, and is customary in nucleotide chemistry, or which does not occur naturally, or its prodrug form;

D is, independently of any other D, a group (CR₃R₄)_t, wherein t is from 2 to 10;

E is, independently of any other E, a group (CR₅R₆)_{u'},

R₅ and R₆ are, independently of each other, a radical consisting of hydrogen, C₁-C₆-alkyl, or the radical of an amino acid side chain, wherein adjacent R₅ and R₆ radicals can form a C₅-C₈-cycloalkyl ring or a spiro compound;

wherein R₁, R₂, R₃, R₄, and u' are as defined above;

and physiologically tolerated salts of the PNA derivative of Formula I,

with the provisos that at least one Y, Y', Z, or Z' radical is hydroxyl, mercapto, oxyanion, or thioate, and that at least one B radical is a nucleobase.

4. A PNA derivative as claimed in claim 3, wherein at least one Y, Y', Z, or Z' radical in Formula I is oxyanion or thioate in a pH range from 4.5 to 14.

5. A PNA derivative as claimed in claim 3, wherein n and m are 0.

6. A PNA derivative as claimed in claim 3, wherein q is 1.

7. A PNA derivative as claimed in claim 3, wherein W and W' are oxygen.

8. A PNA derivative as claimed in claim 3, wherein Y and Y' are hydroxyl or oxyanion.
9. A PNA derivative as claimed in claim 3, wherein V and V' are oxygen.
10. A PNA derivative as claimed in claim 3, wherein X and X' are, independently of each other, U-(C₂-C₂₂-alkanediyI)-U or U-(CH₂CH₂-O)u', wherein u' is from 1 to 6.
11. A PNA derivative as claimed in claim 3, wherein X, X', Z, and Z' are, independently of each other, fluorescein, rhodamine, TAMRA or cyanine dye, biotin, dabcyl, psoralen, acridine, DNP, cholesterol, vitamin E, dabcyl, edans, lexitropsin, psoralen, BODIPY, ROX, or an R6G or digoxygenin radical.
12. A PNA derivative as claimed in claim 3, wherein X, X', Z, and Z' are, independently of each other, a monophosphate, a biotin derivative, or a fluorescein derivative.
13. A PNA derivative as claimed in claim 3, wherein Z is a fluorescence label and Z' is a quencher.
14. A PNA derivative as claimed in claims 3, wherein Z is a quencher and Z' is a fluorescence label.
15. A PNA derivative as claimed in claim 3, wherein Z and Z' are, independently of each other, a C₁-C₂₂-alkyl radical, a C₁-C₂₂-U radical, hydroxy-C₁-C₁₈-U, an aminoalkyl-U radical, a group of the Formula

R₇-(CH₂CH₂-O)_m, wherein R₇ is OH or NH₂ and m is from 1 to 6, or a mercaptoalkyl-V radical.

16. A PNA derivative as claimed in claim 3, wherein q is 0.
17. A PNA derivative as claimed in claim 16, wherein D' is acylamino.
18. A PNA derivative as claimed in claim 3, wherein D is (CH₂)_t.
19. A PNA derivative as claimed in claim 3, wherein A, E, and G are CH₂.
20. A PNA derivative as claimed in claim 3, wherein B is adenine, cytosine, 5-methylcytosine, guanine, thymine, uracil, purine, 2,6-diaminopurine, N⁴N⁴-ethanocytosine, N⁶N⁶-ethano-2,6-diaminopurine, 5-(C₃-C₆)-alkynyluracil, 5-(C₃-C₆)-alkynyl-cytosine, 5-(1-propargylamino)uracil, 5-(1-propargylamino)cytosine, phenoxazine, 9-aminoethoxyphenoxazine, 5-fluorouracil or pseudouracil, 5-(hydroxymethyl)uracil, 5-aminouracil, pseudouracil, dihydrouracil, 5-(C₁-C₆)-alkyluracil, 5-(C₁-C₆)-alkyl-cytosine, 5-(C₂-C₆)-alkenylcytosine, 5-fluorocytosine, 5-chlorouracil, 5-chlorocytosine, 5-bromouracil, 5-bromocytosine, 7-deazaadenine, 7-deazaguanine, 8-azapurine, or a 7-deaza-7-substituted purine.
21. A PNA derivative as claimed in claim 3, wherein {POLY} comprises a nucleotide base sequence binds to at least one sequence of at least one tumor suppressor gene, oncogene, or telomerase, or to their mRNA transcription products.

- PCT/US2003/036660
22. A PNA derivative as claimed in claim 21, wherein the base sequence of the PNA moiety binds to the translation start of HA-ras mRNA.
 23. A pharmaceutical comprising the PNA derivative as claimed in claim 1 and a physiologically acceptable carrier or excipient.
 24. A pharmaceutical comprising the PNA derivative as claimed in claim 3 and a physiologically acceptable carrier or excipient.
 25. A PNA derivative as claimed in claim 1, wherein the PNA derivative is a diagnostic agent.
 26. A method for detecting a nucleic acid of interest, said method comprising
 - labeling a PNA derivative as claimed in claim 1 with a detectable label, wherein the PNA derivative comprises a base sequence that hybridizes with at least one sequence present in the nucleic acid of interest under selected conditions,
 - combining said labeled PNA derivative with a sample suspected of containing the nucleic acid of interest, and
 - detecting specific binding of said labeled PNA derivative to said nucleic acid of interest,wherein specific binding indicates the presence of the nucleic acid of interest in the sample.
 27. The method of claim 25, wherein the method further comprises quantifying the detected nucleic acids.
 28. The method of claim 25, wherein the nucleic acid of interest is a nucleic acid of a microorganism or a virus.

29. The method of claim 25, wherein the method is fluorescence in-situ hybridization (FISH).
30. The PNA derivative as claimed in claim 1, wherein the PNA derivative is an antisense agent, anti-gene agent, decoy agent, or chimeraplast agent.
31. A PNA chip comprising a PNA derivative as claimed in claim 1 and a substrate suitable for fabricating a microarray.
32. A biosensor comprising a PNA derivative as claimed in claim 1 and a substrate suitable for conducting a signal from the PNA derivative to a detection device.
33. A process for preparing a PNA derivative of Formula I in which q is 0, said process comprising
- linking the C-terminus of an amidonucleic acid, which is optionally N-terminally protected, to a solid phase-bound phosphorylating reagent, or binding an amidonucleic acid which is phosphorylated C-terminally to a solid support,
 - optionally, extending the backbone of the PNA oligomer by sequentially coupling with amidonucleic acid monomers, and
 - optionally, deprotecting the N-terminus of the PNA oligomer.
34. The process as claimed in claim 33, wherein the PNA is prepared using t-butyloxycarbonyl (BOC), 9-fluorenylmethoxycarbonyl (Fmoc), or monomethoxytrityl (Mmt) protecting groups.
35. The process as claimed in claim 33, wherein the PNA is prepared using solid supports.

- T O C T H E P A T E N T
36. The process as claimed in claim 35, wherein CPG, tentagel, or aminomethylpolystyrene is used as the solid support.
 37. The process for preparing a PNA derivative of the Formula I as claimed in claim 33, further comprising purifying the PNA derivative using chromatography or electrophoresis.
 38. The process as claimed in claim 37, wherein the PNA derivative is purified using chromatography using a basic stationary phase and a gradient of an acid or salt-containing eluent.
 39. The process as claimed in claim 38, wherein the stationary phase is an anion exchanger or a mixed-mode phase.
 40. The PNA derivative as claimed in claim 1, wherein the phosphoryl radical is a hydroxyl group or a mercapto group.
 41. The PNA derivative as claimed in claim 1, wherein at least one of the phosphoryl radicals carries one or more hydroxyl or mercapto groups, which is/are deprotonatable in a pH range from 4.5 to 14.
 42. The PNA derivative as claimed in claim 41, wherein said one or more hydroxyl or mercapto groups is/are deprotonatable in a pH range from 6.5 to 12.
 43. The PNA derivative as claimed in claim 41, wherein said one or more hydroxyl or mercapto groups is/are deprotonatable in a pH range from 6.5 to 9.
 44. The PNA derivative as claimed in claim 1, wherein the phosphoryl radical is a phosphate, a phosphonate, a thiophosphate, a

phosphoamidate, or a substituted phosphoryl radical, and wherein substituted phosphoryl radicals carry, where appropriate, one or more labeling groups, groups for crosslinking, groups which promote intracellular uptake, or groups which increase the binding affinity of the PNA derivative for nucleic acids.

45. The PNA derivative as claimed in claim 3, wherein u' is from 1 to 4.
46. The PNA derivative as claimed in claim 3, wherein u' is 1.
47. The PNA derivative as claimed in claim 3, wherein X, X', or both are, a bifunctional fluorescein, rhodamine, TAMRA, biotin, pyrene, dinitrophenyl, cholesteryl, acridine, adamantyl, vitamin E, cyanine dye, dabcyl, edans, lexitropsin, psoralen, BODIPY, ROX, R6G, or digoxigenin radical.
48. The PNA derivative as claimed in claim 3, wherein m' is from 2 to 10.
49. The PNA derivative as claimed in claim 3, wherein Z, Z', or both are a monofunctional or bifunctional fluorescein, rhodamine, TAMRA, biotin, pyrene, dinitrophenyl, cholesteryl, acridine, adamantyl, vitamin E, cyanine dye, dabcyl, edans, lexitropsin, psoralen, BODIPY, ROX, R6G, or digoxigenin radical.
50. The PNA derivative as claimed in claim 3, wherein R₁, R₂, or both are hydrogen.
51. The PNA derivative as claimed in claim 3, wherein R₃, R₄, or both are hydrogen.
52. The PNA derivative as claimed in claim 3, wherein n is from 0 to 3.

65. The PNA derivative as claimed in claim 10, wherein X and X' are O-(CH₂)₂-O.
66. The PNA derivative as claimed in claim 10, wherein X and X' are U-(CH₂CH₂-O)_{u'}, wherein u' is from 1 to 6.
67. The PNA derivative as claimed in claim 10, wherein X and X' are O(CH₂CH₂-O)_{u''}, wherein u' is from 1 to 6.
68. The PNA derivative as claimed in claim 15, wherein Z and Z' are, independently of each other, a C₁-C₂₂-alkoxy radical.
69. The PNA derivative as claimed in claim 15, wherein Z and Z' are, independently of each other, C₁₆-alkoxy.
70. The PNA derivative as claimed in claim 15, wherein Z and Z' are, independently of each other, hydroxy-C₁-C₁₈-O.
71. The PNA derivative as claimed in claim 15, wherein Z and Z' are, independently of each other, HO-(CH₂)₃₋₁₂O.
72. The PNA derivative as claimed in claim 15, wherein Z and Z' are, independently of each other, an aminoalkoxy radical.
73. The PNA derivative as claimed in claim 15, wherein Z and Z' are, independently of each other, 6-aminohexoxy or 5-aminopentoxyl.
74. The PNA derivative as claimed in claim 15, wherein Z and Z' are, independently of each other, HO(CH₂CH₂-O)₂.

75. The PNA derivative as claimed in claim 15, wherein Z and Z' are, independently of each other, HO(CH₂CH₂-O)₆.
76. The PNA derivative as claimed in claim 15, wherein Z and Z' are, independently of each other, H₂N-(CH₂CH₂-O)₂.
77. The PNA derivative as claimed in claim 15, wherein Z and Z' are, independently of each other, a mercaptoalkoxy radical.
78. The PNA derivative as claimed in claim 15, wherein Z and Z' are, independently of each other, 6-mercaptophexyloxy.
79. The PNA derivative as claimed in claim 17, wherein D' is acetylamino.
80. The PNA derivative as claimed in claim 15, wherein D is (CH₂)₂.
81. A process for preparing a PNA derivative of Formula I in which q is 1, said process comprising
 - a) linking the C-terminus of an amidonucleic acid, which is optionally N-terminally protected, to a solid phase-bound phosphorylating reagent, or binding an amidonucleic acid which is phosphorylated C-terminally to a solid support,
 - b) optionally, extending the backbone of the PNA oligomer by sequentially coupling with amidonucleic acid monomers,
 - c) optionally, deprotecting the N-terminally protected PNA backbone,
 - d) coupling a phosphorus (III) or a phosphorus (IV) group to the N-terminus of the PNA backbone using activated phosphorylating reagents optionally containing a spacer,

- e) optionally, repeating step d), and
- f) optionally, oxidizing the phosphorus (III) group to a phosphorus (V) group.